UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/315,292	05/20/1999	CLARENCE FRANK BENNETT	ISIS-3561	6344

32650 7590 08/25/2003

WOODCOCK WASHBURN LLP
ONE LIBERTY PLACE - 46TH FLOOR
PHILADELPHIA, PA 19103

EXAMINER
ZARA, JANE J

ART UNIT	PAPER NUMBER
1635	23

DATE MAILED: 08/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/315,292	Bennett et al.
Examiner	**Art Unit**
Jane Zara	1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on *Apr 18, 2002*.

2a) ☐ This action is **FINAL**. 2b) X This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) X Claim(s) *37, 39-49, 51-59, 61, 63, and 64* is/are pending in the application.

4a) Of the above, claim(s) *39-41, 43, 52, 53, 59, and 64* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) X Claim(s) *37, 42, 44-49, 51, 54-58, 61, and 63* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) X Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)	☐ Notice of References Cited (PTO-892)	4)	☐ Interview Summary (PTO-413) Paper No(s).
2)	☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5)	☐ Notice of Informal Patent Application (PTO-152)
3)	X Information Disclosure Statement(s) (PTO-1449) Paper No(s). 14	6)	☐ Other:

DETAILED ACTION

This Office action is in response to the communications filed January 18, 2002 and April 18, 2002, Paper Nos: 19 and 22 respectively.

Claims 37, 39-49, 51-59, 61, 63 and 64 are pending in the instant application.

Any rejections not repeated in this Office action are hereby withdrawn.

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 18, 2002 has been entered.

Election/Restriction

Newly submitted claims 52, 53, 59 and 64 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The elected invention is drawn to methods of administration of antisense oligonucleotides to the lung of a subject; claim 52 is drawn to a method of treating an animal; claim 53 is drawn to a metho of investigating the role of a gene or gene product; claim 59 is drawn to a method of gene modulation in an animal.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 52, 53 and 59 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Applicants' election with traverse of Group II, phosphorothioate linkages, and SEQ ID NO: 1, corresponding to antisense targeting ICAM-1 in Paper No. 6, filed March 30, 2000, is acknowledged as set forth in the Office action mailed March 24, 2000, Paper No. 8. Claims 39-41 and 43 are withdrawn from consideration as they are drawn to non-elected species, and elected claims 37, 42, 44-49, 51, 54-58, 61 and 63 are examined on their merits set forth in the Office action below.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: The disclosure of particularized methods, devices and compositions comprising the various nucleotide sequences (e.g. SEQ ID NOS: 1-10) were not made in the claimed parent applications, consequently, the priority awarded for the instant application is May 20, 1999. Applicants assert that the prophetic disclosure of inhalation made in the claimed priority document 07/801,168, combined with articles provided in the declaration by Applicant in the instant application, filed May 23, 2001, Paper No. 16, describing the administration of various (e.g. non-nucleic acid) compositions, including those presumably historically enabled since the 19th century, provide for the priority claimed. Contrary to

applicants' assertions, the cited historical documents, combined with prophetic disclosures in the claimed priority documents of pharmaceutical formulations, do not compensate for the lack of substantive disclosures required for attaining priority of claimed parent applications. Contrary to Applicants assertions, the historical review of prior administration of various reagents (non-nucleic acid) to the lungs is not a disclosure of the administration and subsequent lung delivery of aerosolized antisense oligonucleotides, nor of utilizing medical devices to perform such lung delivery.

Applicants assert that the priority documents disclose the phrases that include the terms "oligonucleotides may be formulated in a pharmaceutical composition", which are then intended to be "administered in a number of ways depending on whether local or systemic treatment is desired...", and includes the term "inhalation". Contrary to Applicants assertions, the disclosure of the term inhalation, and pharmaceutical composition, does not substitute for the disclosure of lung delivery of antisense oligonucleotides using aerosolized or nebulized oligonucleotides. No disclosure of these processes, nor of oligonucleotide sequences have been made in the priority documents.

Response to Arguments and Amendments

Applicant's arguments with respect to claims 37-59, 61, 63 and 64 have been considered but are moot in view of the new ground(s) of rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 37, 42, 44-49, 51, 54-58, 61 and 63 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 30-34, 36, 39, 43-46, 50, 52, 53 and 55-83 of copending Application No. 09/315,581. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed inventions in both applications are drawn to methods and compositions comprising the administration of antisense oligonucleotides (including those of the same nucleotide sequences) to

the lungs of an organism. The inventions differ regarding the modifications that are incorporated into the oligonucleotides (e.g. sugar and internucleotide modifications).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37, 42, 44-49, 41, 54-58, 61 and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of claim 37, lines 4-7, and claim 54, lines 3-6, which recite the negative limitation of at least one sugar moiety of at least one nucleoside unit ... is not a 2'-deoxyribofuranosyl sugar moiety or at least one internucleotide linkage is not a phosphodiester or a phosphorothioate linkage, cannot be determined. Appropriate clarification is requested.

Claim 42 depends from claim 39, which depends from claim 38, which has been canceled. Appropriate correction is requested.

In claim 56, lines 1 and 2, the metes and bounds of an animal suspected to suffer from a disease or disorder cannot be determined. Clarification is requested.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37, 42, 44-49, 41, 54-58, 61 and 63 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to antisense oligonucleotides comprising at least one sugar moiety of at least one nucleoside unit that is not a 2'-deoxyribofuranosyl sugar moiety or at least one internucleotide linkage that is not a phosphodiester or a phosphorothioate linkage. The specification and claims do not indicate the elements that are essential to the claimed invention, drawn to antisense oligonucleotides comprising at least one sugar moiety of at least one nucleoside unit that is not a 2'-deoxyribofuranosyl sugar moiety or at least one internucleotide linkage that is not a phosphodiester or a phosphorothioate linkage. The specification and claims do not indicate the distinguishing features and attributes that are concisely shared by genus members comprising antisense oligonucleotides comprising at least one sugar moiety of at least one nucleoside unit that is not a 2'-deoxyribofuranosyl sugar moiety or at least one internucleotide linkage that is not a phosphodiester or a phosphorothioate linkage. The scope of the claims includes numerous structural variants, and the genus is highly variant, because a significant number of structural differences between members of the genus is permitted. Concise structural features that could distinguish structures or compounds within the genus from others is missing

from the disclosure and the claims. One of skill in the art would reasonably conclude that the description provided in inadequate, and that Applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 37, 42, 44-49, 51, 54-58 and 61 are rejected under 35 U.S.C. 102(e) as being anticipated by Unger et al.

Unger et al (USPN 5,733,572) teach devices, compositions and methods of administration of antisense oligonucleotide therapeutic or diagnostic compositions comprising administration of

one or more antisense oligonucleotides to a subject suffering from asthma or other lung associated disease or condition, wherein the sugar moiety of at least one nucleoside unit of each antisense is not a 2'-deoxyribofuranosyl sugar moiety or at least one internucleotide linkage within said antisense is not a phosphorothioate or phosphodiester linkage, wherein water or physiological saline in the aerosol (nebulized) compositions of Unger et al for therapeutic delivery directly into the lung comprises sterilized, pyrogen free water, which antisense is optionally in powder form (see especially col. 1, 3, 4, 7, 19, 22, 31, 32, 40, 41 and 49).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 63 is rejected under 35 U.S.C. 103(a) as being unpatentable over Unger et al in view of Bennett et al.

The claim is drawn to a method of administration of an antisense oligonucleotide of SEQ ID NO: 1, comprising aerosolizing the antisense and introducing the antisense into the lungs of a subject, wherein the sugar moiety of at least one nucleoside unit of the antisense is not a 2'-deoxyribofuranosyl sugar moiety or at least one internucleotide linkage within said antisense is not a phosphorothioate or phosphodiester linkage.

Unger is relied upon as cited in the 102 rejection above.

Unger does not teach the administration of antisense of SEQ ID NO: 1.

. Bennett et al (USPN 5514,788) teach methods of administration of antisense oligonucleotide of SEQ ID NO: 1, for inhibition of target gene ICAM-1 expression (See SEQ ID NO: 22 and accompanying alignment data; col. 7-8; col. 23-27).

It would have been obvious to one of ordinary skill in the art to administer the antisense oligonucleotide comprising SEQ ID NO: 1 to inhibit target gene expression because the design and targeting of ICAM-1 had been taught previously by Bennett et al using SEQ ID NO: 1. One of ordinary skill in the art would have been motivated to administer this antisense in nebulized form for lung delivery because Unger teaches the ability to deliver nebulized antisense oligonucleotides to the lungs of subjects and ICAM-1 has been taught to be involved in various inflammatory processes, and one would be motivated to deliver antisense targeting ICAM-1 to the lungs to diminish inflammatory processes occurring in the lungs due to overexpression of ICAM-1

One of ordinary skill in the art would have expected that this antisense oligonucleotide is successfully delivered to lung cells because Unger teaches the ability to deliver aerosolized antisense oligonucleotides to target cells in the lungs.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art.

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JZ

August 20, 2003

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER